Toxic Breastmilk? Breastfeeding and Substance Use Disorders

Abby Montague, MD

April 5, 2024

Disclosures

- No financial relationships
- Pictures are cited or the property of the presenter

Objectives

- Understand benefits of breastfeeding
- Describe the process of drug transfer into human milk
- Discuss the literature around drug excretion and potential infant toxicity for several substances
- Begin to develop a harm reduction approach to counseling breastfeeding parents with substance use disorders

Breastfeeding benefits

TABLE 2 Breastfeeding and Infant Outcomes[a]

Outcome and Reference	% Lower Risk	Breastfeeding[a]	Compared With:
SIDS[87]	40	2–4 mo	None
	60	4–6 mo	None
	64	>6 mo	None
Infant mortality, United States[88]	19	Ever	Never
Neonatal mortality (8–27 d)[88]	51	Ever	Never
Postneonatal mortality[8]	21	Ever	Never
	38	>3 mo	Never
Infant mortality (7–365 d)[9]	26	Ever	Never

Meek 2022

Breastfeeding benefits

TABLE 2 Breastfeeding and Infant Outcomes[a]

Outcome and Reference	% Lower Risk	Breastfeeding[a]	Compared With:
Lower respiratory tract infection[91]	19	Exclusive 6 mo	Exclusive <4 mo
Severe or persistent diarrhea[91]	30	Exclusive 6 mo	Exclusive <4 mo
Otitis media[92]	33	Ever	Never
	33	More	Less
	43	Exclusive 6 mo	None
Asthma 5–18 y[93]	10	More	Less
	12	Ever	Never
Asthma ever, all ages[94]	22	Longer	Shorter

Meek 2022

Breastfeeding benefits

Baby

- Decreased mortality, SIDS
- Decreased infections
- Decreased chronic diseases

Parent

- Decreased diabetes and HTN
- Decreased cancer

Meek 2022

Contraindications to breastfeeding

- Classic galactosemia
- Maternal infections
  - HIV (in the US)
  - Human T-cell lymphotropic virus
  - Untreated brucellosis
  - Ebola virus
  - Hep C with cracked or bleeding nipples
  - HSV if lesions cannot be covered
- Illicit substance use

Meek 2022

Drug transfer into human milk

American Academy of Pediatrics
Section on Breastfeeding

- Factors favoring excretion into milk
  - ↓ Molecular weight
  - ↓ Protein binding
  - ↑ Lipophilicity
  - ↑ pKa
  - ↑ Efflux transporter affinity

Ito 2018

Infant dose

- Absolute infant dose (AID) is amount in mg/kg/day based on average milk concentration and infant milk intake

- Relative infant dose (RID) the percent of parent's therapeutic dose the infant receives
  - Daily milk intake, M:P ratio, maternal plasma concentration
  - Plasma concentration depends on dose, bioavailability, dosing interval, and total body clearance.
  - Infant tolerance depends on bioavailability, clearance, and susceptibility

Ito 2017

Organization Recommendations

- American Academy of Pediatrics
- Academy of Breastfeeding Medicine
- American College of Obstetrics and Gynecology
- Centers for Disease Control and Prevention
- SAMSA

- Recommend BF in women with OUD in remission
- Cautious monitoring when on sedating substances
- Contraindicated with active illicit substance use

Organization Recommendations

- **World Health Organization**
  - ". . . encouraged to breastfeed unless the risks clearly outweigh the benefits"
  - ". . . Advised and supported to cease alcohol or drug use; however, substance use is not necessarily a contraindication to breastfeeding"

WHO 2014

Side note: Impaired parenting

Safe or Safer?

Wikimedia commons

Roadmap

Clinical scenarios with drugs of interest

- Amount
- Toxicity
- Duration

Scenario

- Out to dinner with a friend who just had a baby
- “Oh I know I just need to pump and dump if I drink too much.”

History

https://beersnobsquad.wordpress.com/2015/08/06/vintage-beer-ads-blatz-edition/

https://juxtintime.wordpress.com/2014/04/30/beer-for-breastfeeding-mothers/

Mannella & Beauchamp 1993

Haastrup et al 2013

Alcohol

Amount

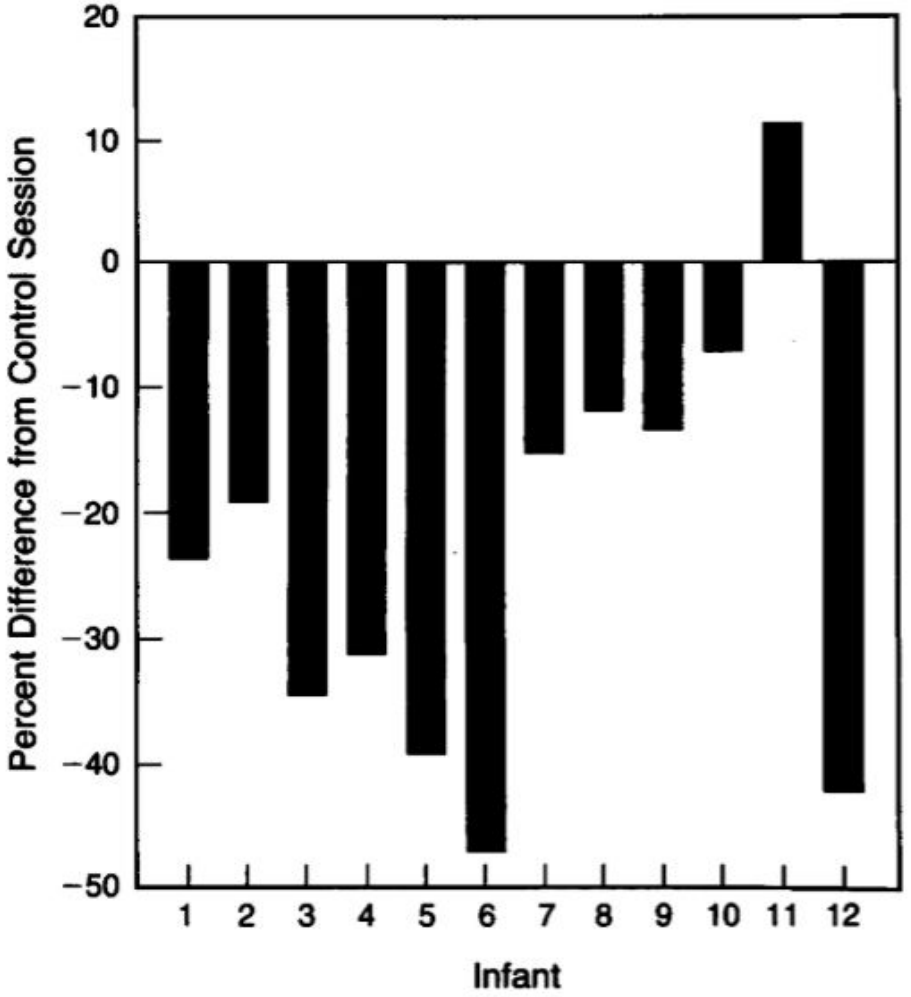
- M:P about 1
  - Mirrored concentration curves
- Mannela & Beauchamp
  - RID about 1.9% (range 0.5%-3.3%)
  - AID 5.1 mg/kg (range 1.6-9.9)
- Parent has 4 drinks, feeds baby at Tmax, baby BAL 0.005%

Mannella & Beauchamp 1991 & 1993
Haastrup 2013, Lawton 1985

Alcohol

Toxicity

- Decreased volume of milk intake

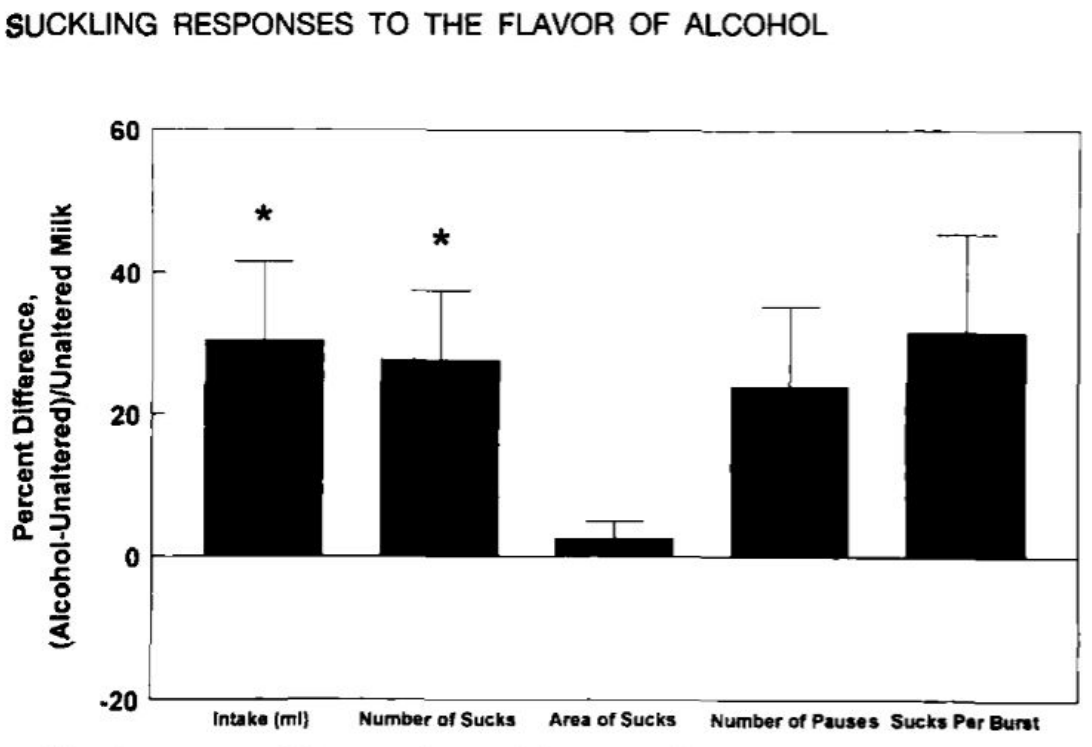


Mannella & Beauchamp 1991 & 1993

Alcohol

Toxicity

- ~~Decreased volume of milk intake~~
- Decreased milk transfer



Mannella JA, 1997
Mannella & Beauchamp 1991 & 1993
Haastrup 2014

Alcohol

Toxicity

- ~~Decreased volume of milk intake~~
- Decreased milk transfer
- Sleep disruption

Mannella & Beauchamp 1991 & 1993
Mannella 1997
Manella & Gerrish 1998

Alcohol

Toxicity

- Premie infants getting TPN
  - Intoxicated at .18%, .08%, .02%, and .004%
  - Others with no signs of intoxication at .001% - .02%

FETAL AND NEONATAL MEDICINE Richard E. Behrman, *Editor*

Intravenously induced infantile intoxication with ethanol

Virginia H. Peden, M.D.,* T. James Sammon, M.D., and Dorothea A. Downey, M.D., *St. Louis, Mo.*

Peden 1973

Long-term toxicity?

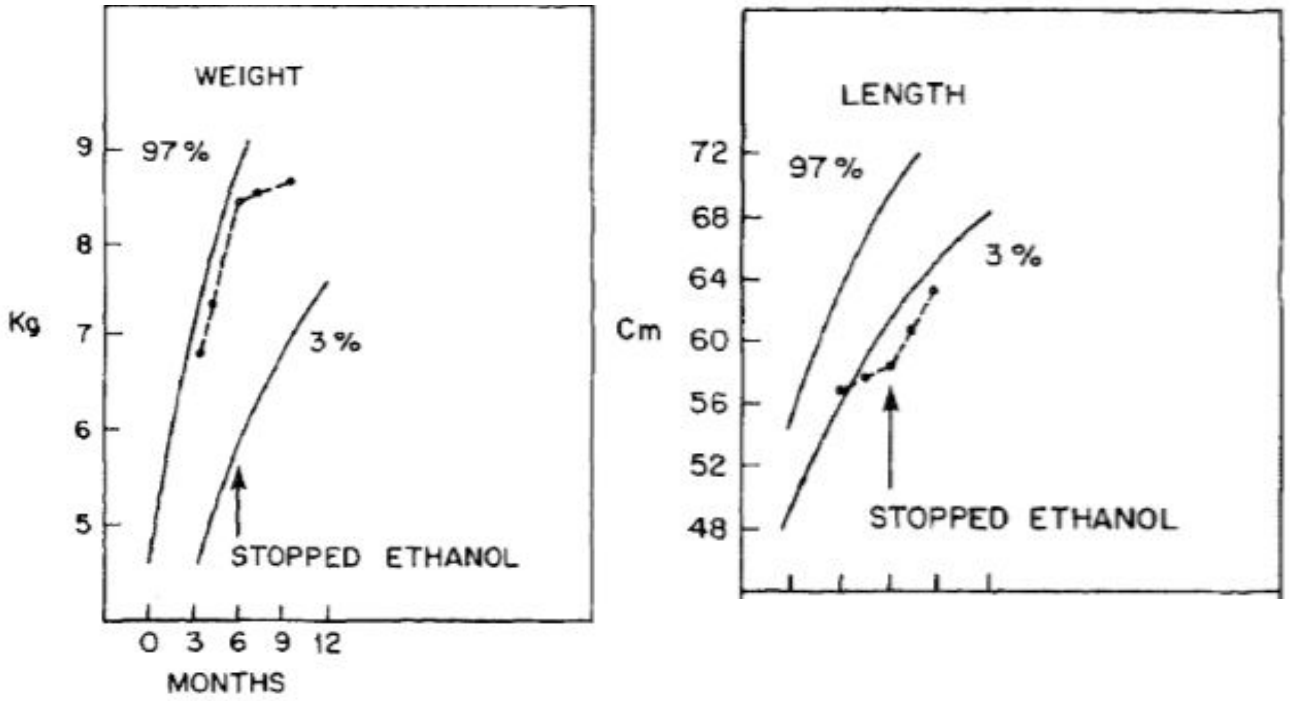


Fig. 1. Reversal of impaired growth and excessive gain in weight on stopping ethanol.

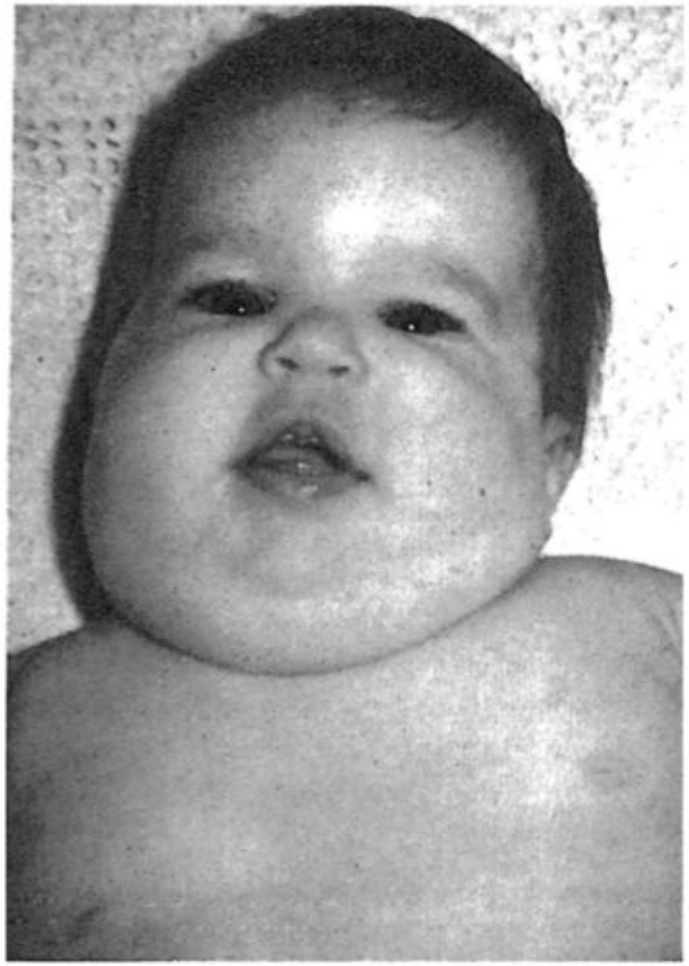


Fig. 2. Cushingoid appearance at 4 months.

Binkiewicz 1978

Long-term toxicity?

- Delayed gross motor development when lactating parent's alcohol intake intake was >1 drink per day

Little 1989

Long-term toxicity?

- ~~Delayed gross motor development~~
- No differences in Ages and Stages Questionnaires
  - Improved personal-social interaction?

Little 2002, Wilson 2017

IMG_3161.JPG

Long-term toxicity?

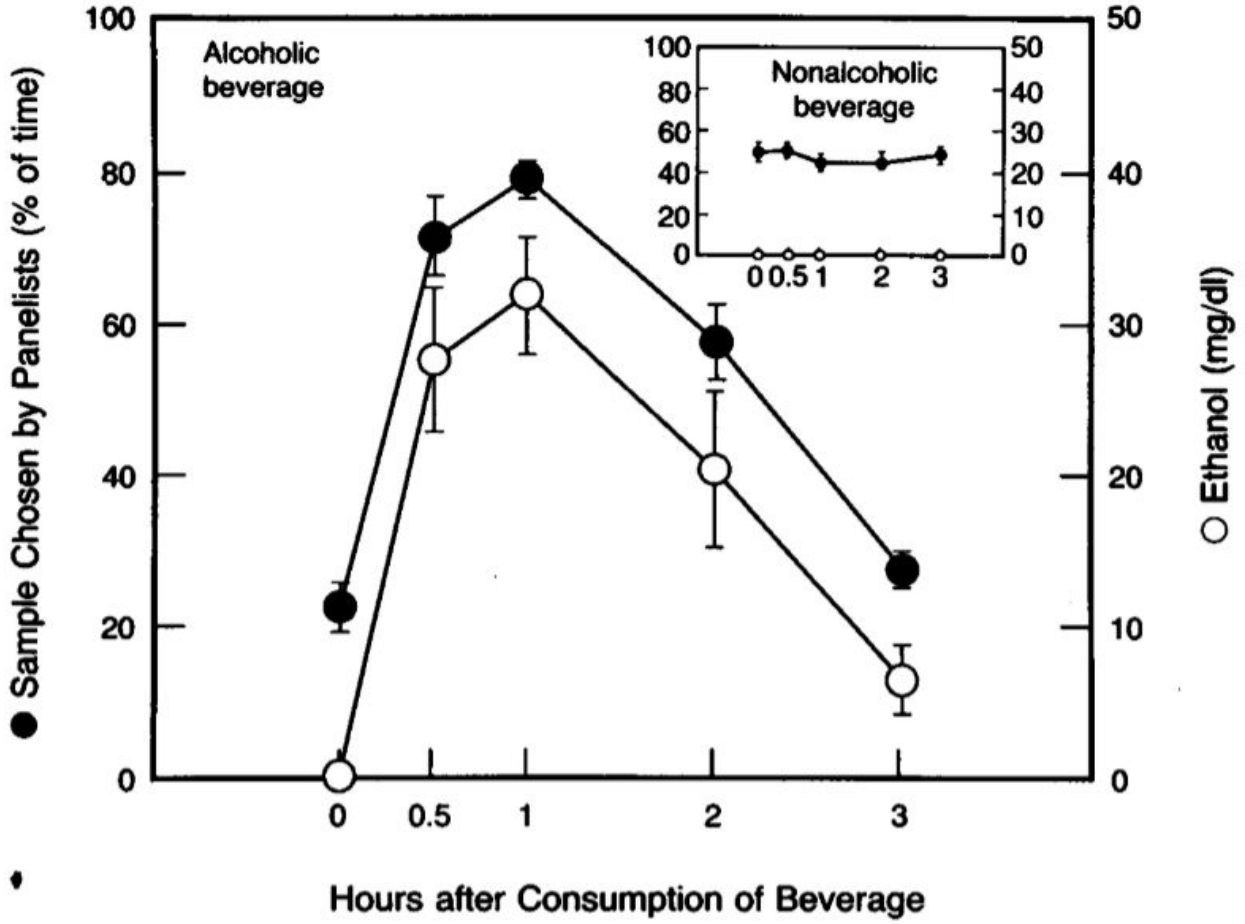
- Decreased nonverbal reasoning in 1st grade
- Decreased composition scores in 3rd grade
- Only spelling deficit persisted to 5th grade
- Poor grammar?
- No increased risk of autism or ADHD

Gibson 2018, 2020, 2022
May 2016, Haastrup 2013

Alcohol

Duration

- Depends!
  - Weight
  - Dose
  - Timing

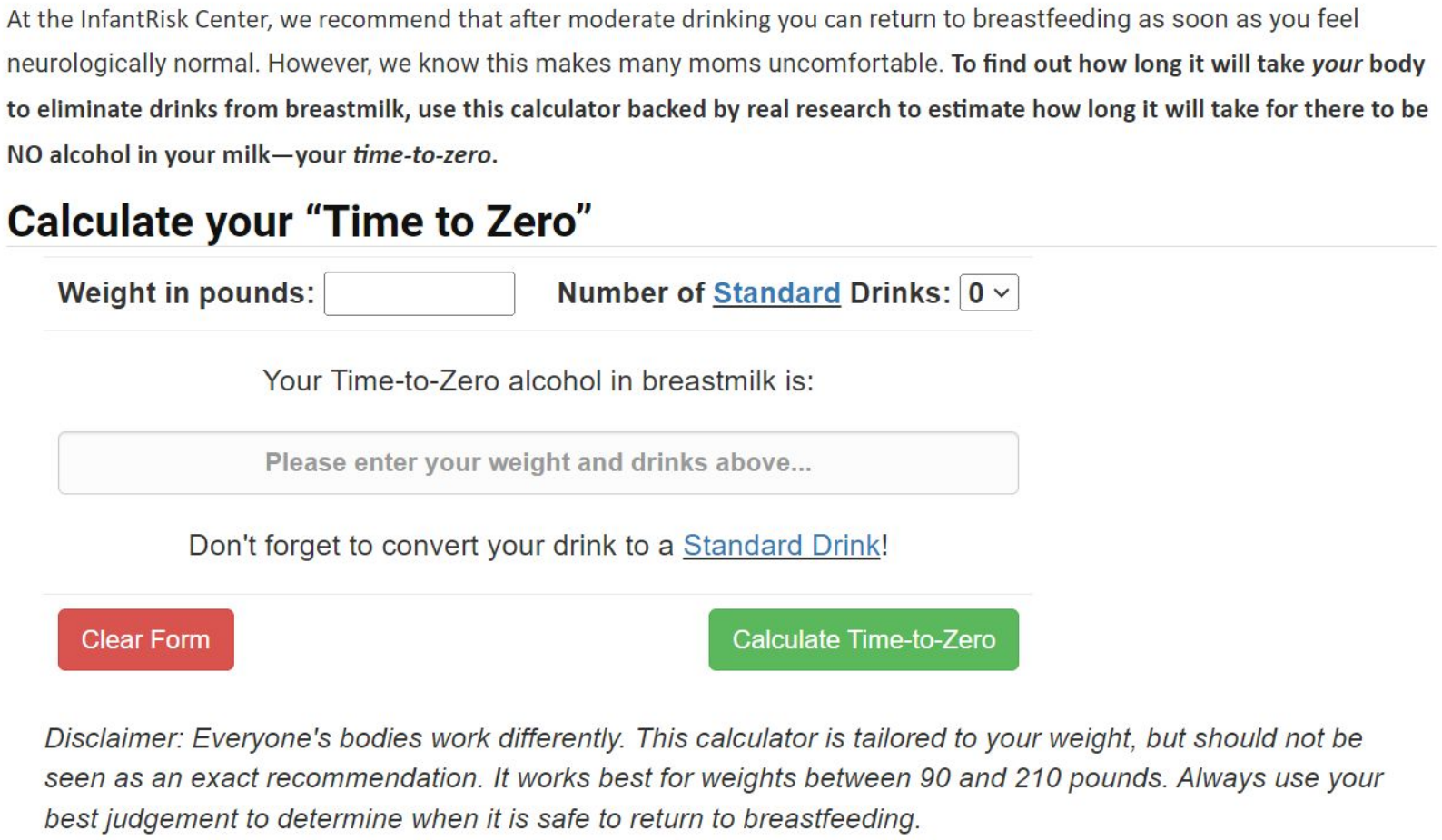


Mennella 1991

Alcohol

Duration

- Depends!
  - Weight
  - Dose
  - Duration



https://infantrisk.com/content/alcohol-breastfeeding-whats-your-time-zero

Alcohol

Duration

- Depends!
  - Weight
  - Dose
  - Duration

At the InfantRisk Center, we recommend that after moderate drinking you can return to breastfeeding as soon as you feel neurologically normal. However, we know this makes many moms uncomfortable. **To find out how long it will take *your* body to eliminate drinks from breastmilk, use this calculator backed by real research to estimate how long it will take for there to be NO alcohol in your milk—your *time-to-zero*.**

Calculate your "Time to Zero"

Weight in pounds: 200 **Number of Standard Drinks:** 4

Your Time-to-Zero alcohol in breastmilk is:

7 hour(s) 36 minutes after 4 drink(s).

Don't forget to convert your drink to a Standard Drink!

Clear Form | Calculate Time-to-Zero

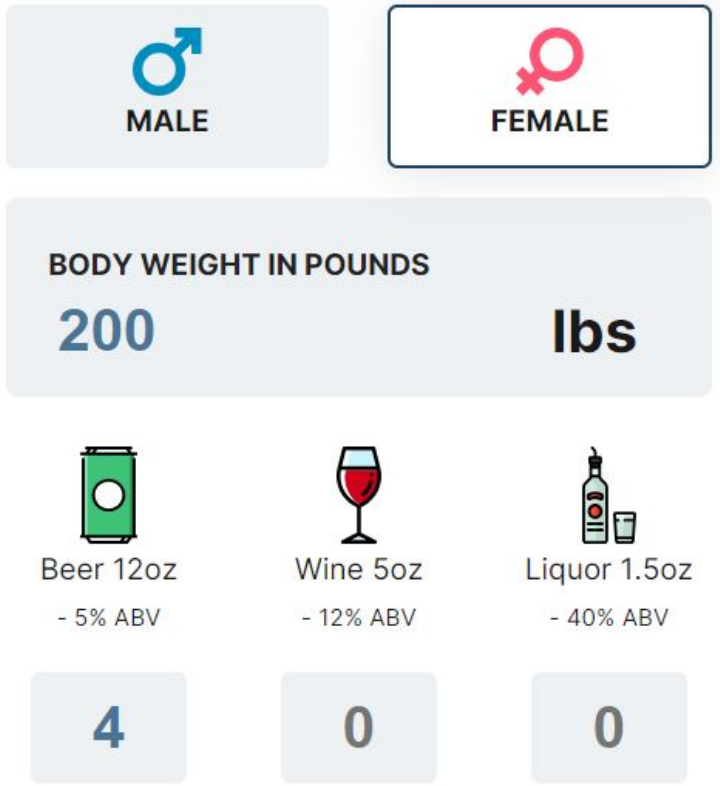
Disclaimer: Everyone's bodies work differently. This calculator is tailored to your weight, but should not be seen as an exact recommendation. It works best for weights between 90 and 210 pounds. Always use your best judgement to determine when it is safe to return to breastfeeding.

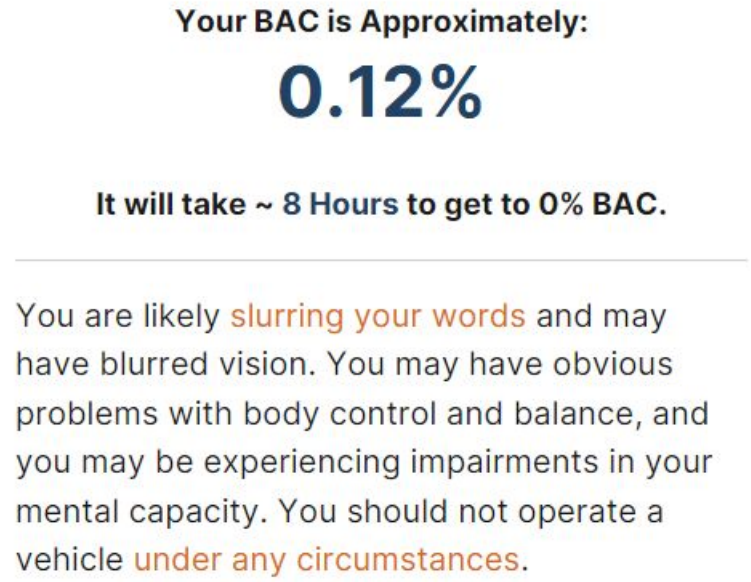
https://infantrisk.com/content/alcohol-breastfeeding-whats-your-time-zero

Alcohol

Duration

- Depends!
  - Weight
  - Dose
  - Duration





4kg baby drinks 4 oz =
BAC 0.005%

https://alcohol.org/bac-calculator/

Scenario

- Mother uses marijuana for anxiety, debating on whether to use after birth vs breastfeeding

Marijuana (Δ9 THC)

Amount

- M:P 6-8
- Baker study – controlled equal dose and timing
  - Median concentration 27.6 ng/ml
  - AID estimated 4-8 mcg/kg/day
  - RID about 2.5% (range 0.4%-8.7%
  - Moss study same median, Josan similar

- Large range in reported AID
  - 1.42 – 48 mcg/kg/day

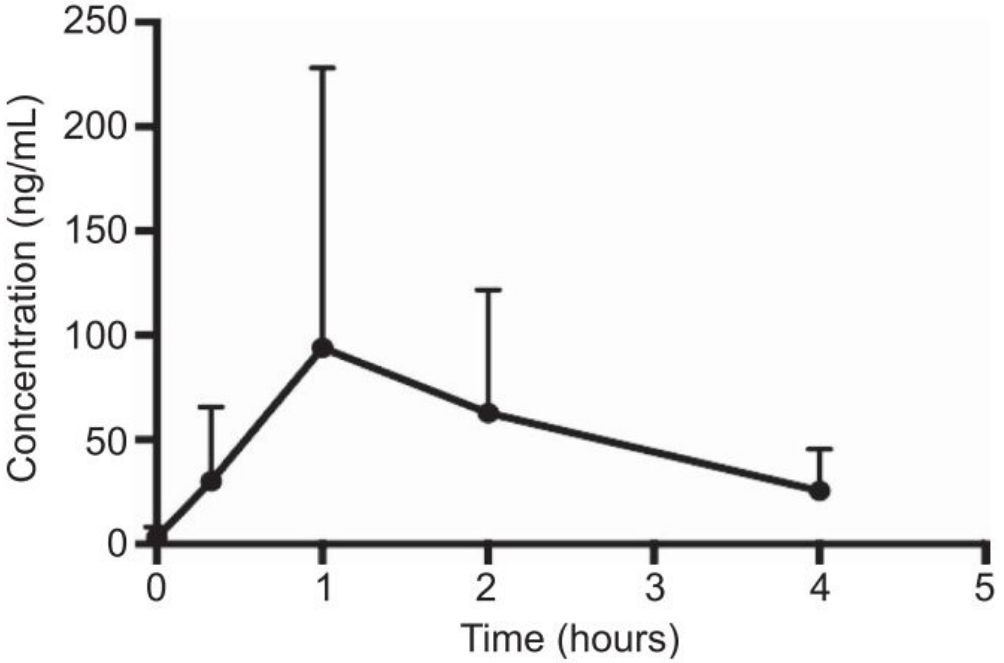


Fig. 2. Mean concentration time profile of delta-9-tetrahydrocannabinol in human breast milk (mean±SD, n=8).

Baker. Inhaled Cannabis in Human Breast Milk. Obstet Gynecol 2018.

Perez-Reyes 1982, Baker 2018, Moss 2021, Bertrand 2018, Josan 2022

Marijuana (Δ9 THC)

Toxicity

- Acute toxicity unlikely (> 1 mg/kg)

Picture: Jennifer Sens for the New York Times (2/2/2017)

Kaczor 2021

Long-term toxicity?

Marijuana: Prenatal and Postnatal Exposure in the Human

Katherine Tennes, M.A., Nanci Avitable, M.A., Carol Blackard, M.D., Cecilia Boyles, M.A., Bernice Hassoun, B.S., Larry Holmes, M.S., and Marie Kreye, Ph.D.

***NIDA Res Monogr Ser*. 1985;NO. 59:48-60.**

No difference + no power = no conclusion

Long-term toxicity?

- Decrease in motor score in infants with THC in breastmilk at one month
- No impact on mental development
- THC concentrations 1/3 of what they are today

Maternal Marijuana Use During Lactation and Infant Development at One Year

SUSAN J. ASTLEY*[1] AND RUTH E. LITTLE†

*Department of Pediatrics, University of Washington, Seattle, WA 98195
†Department of Epidemiology, University of Michigan, Ann Arbor, MI 48109

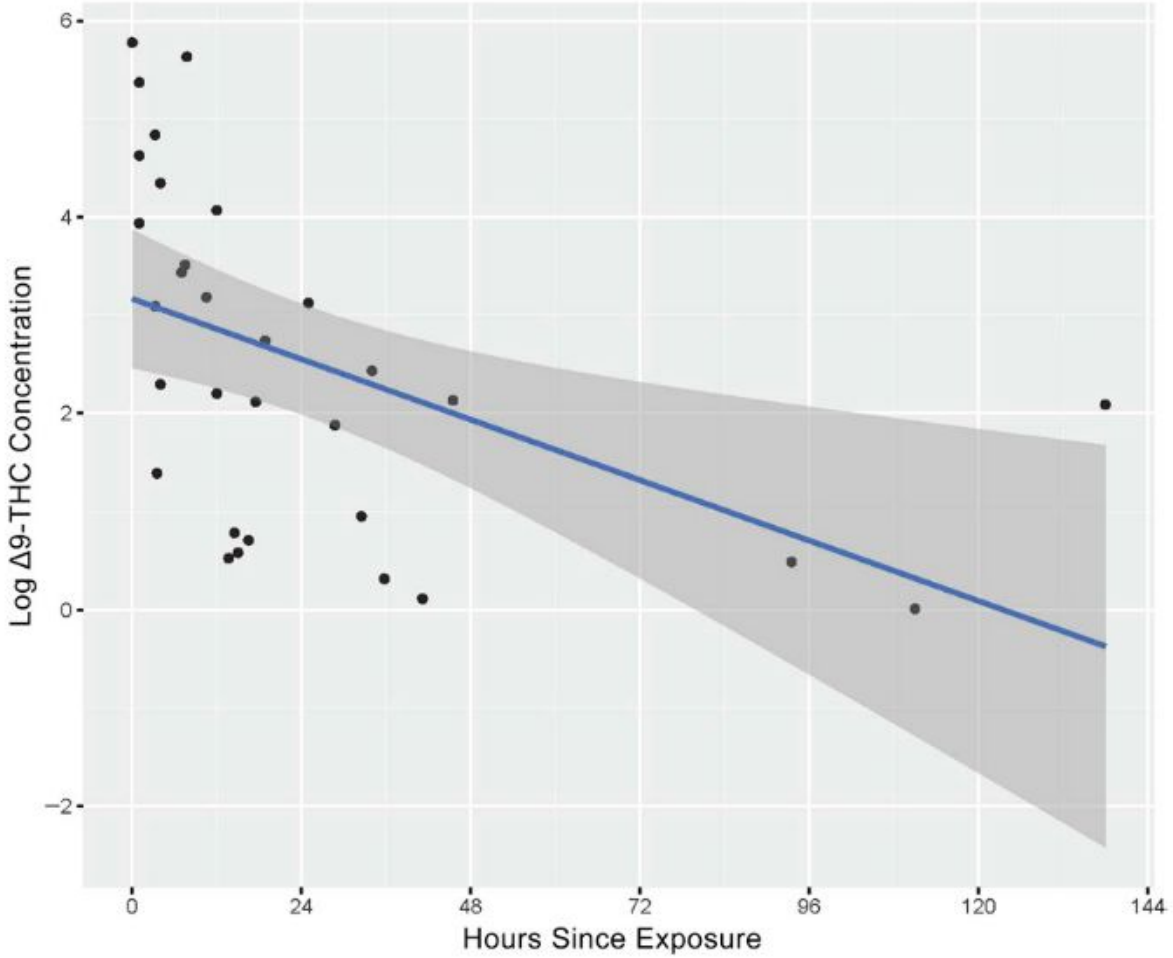
Received 25 May 1989

Neurotoxicol Teratol. 1990;12(2):161-168

Marijuana (Δ9 THC)

Duration

- 6 days



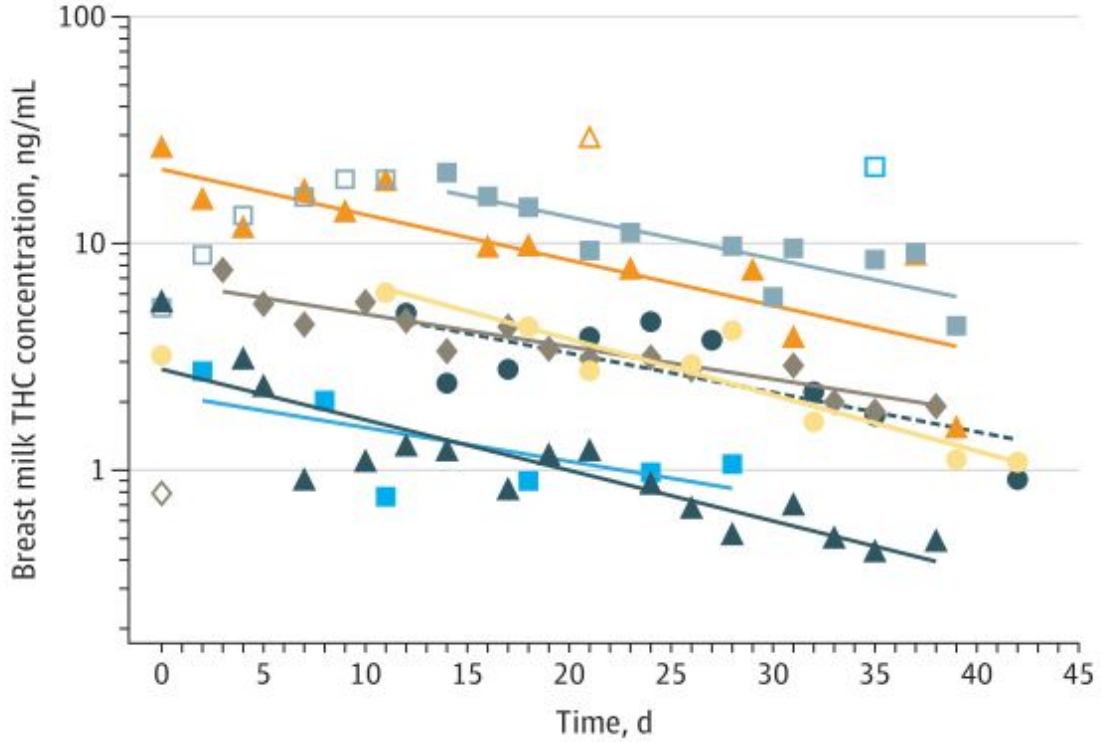
Bertrand 2018

Marijuana (Δ9 THC)

Duration

- > 6 weeks

Figure. Pharmacokinetic Modeling for the Estimated Time to Elimination of Δ-9-Tetrahydrocannabinol (THC) in Breast Milk Following Delivery



Wymore 2021

Clinical Scenario

- Mother with fentanyl use in pregnancy, most recently 7 days ago. Initiated on buprenorphine at that time and plans to enter residential treatment for mothers postpartum.

Fentanyl

Amount

- Steer series: colostrum after C/S or tubal surgery
  - Concentration 0.4 ng/ml
  - AID 0.06 mcg/kg/day
- Nitsun series: mature milk after single dose
  - AID 0.024 mcg/day
  - Collected after 5 hours
- Cohen case report: fentanyl patch
  - Concentration 6.4 ng/mL
  - AID .96 mcg/kg/day (2-3% RID)

- Most data in colostrum
- Data limited to only pharmaceutical use

Steer *et al.*: FENTANYL IN COLOSTRUM

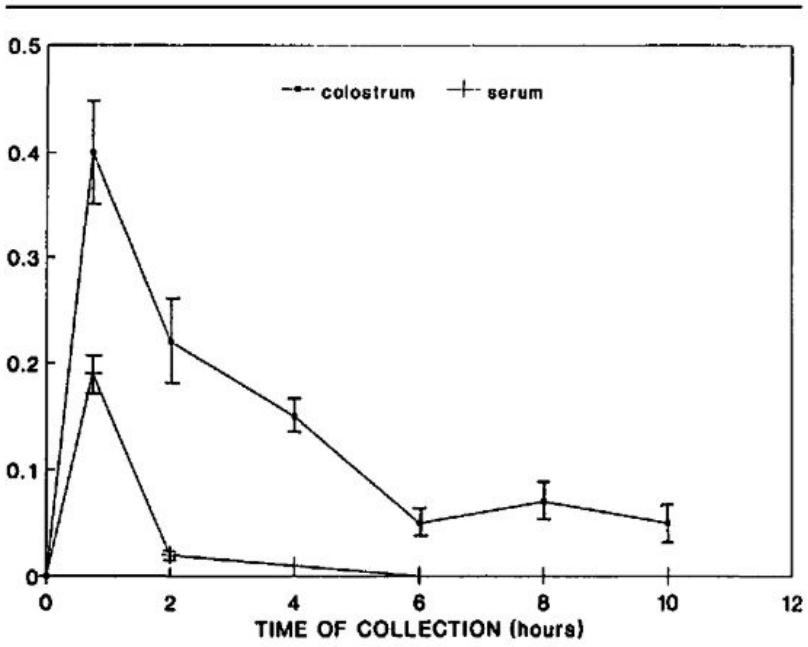


FIGURE Fentanyl concentration in colostrum and serum ($ng \cdot ml^{-1}$) ± standard error of the mean.

Steer 1992, Nitsun 2006, Cohen 2009

Fentanyl

Amount

- High M:P ratio
  - 1.8 -> 11
- Persists longer in milk than plasma
- Higher concentration in chronic use and mature milk
  - Cohen article with patch, breastmilk concentration was 16-fold higher than colostrum study

Steer *et al.*: FENTANYL IN COLOSTRUM

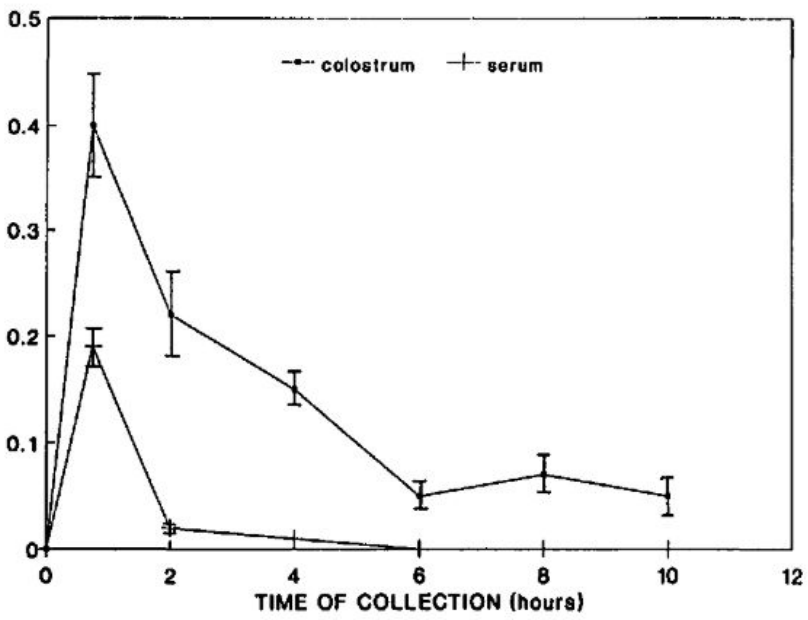


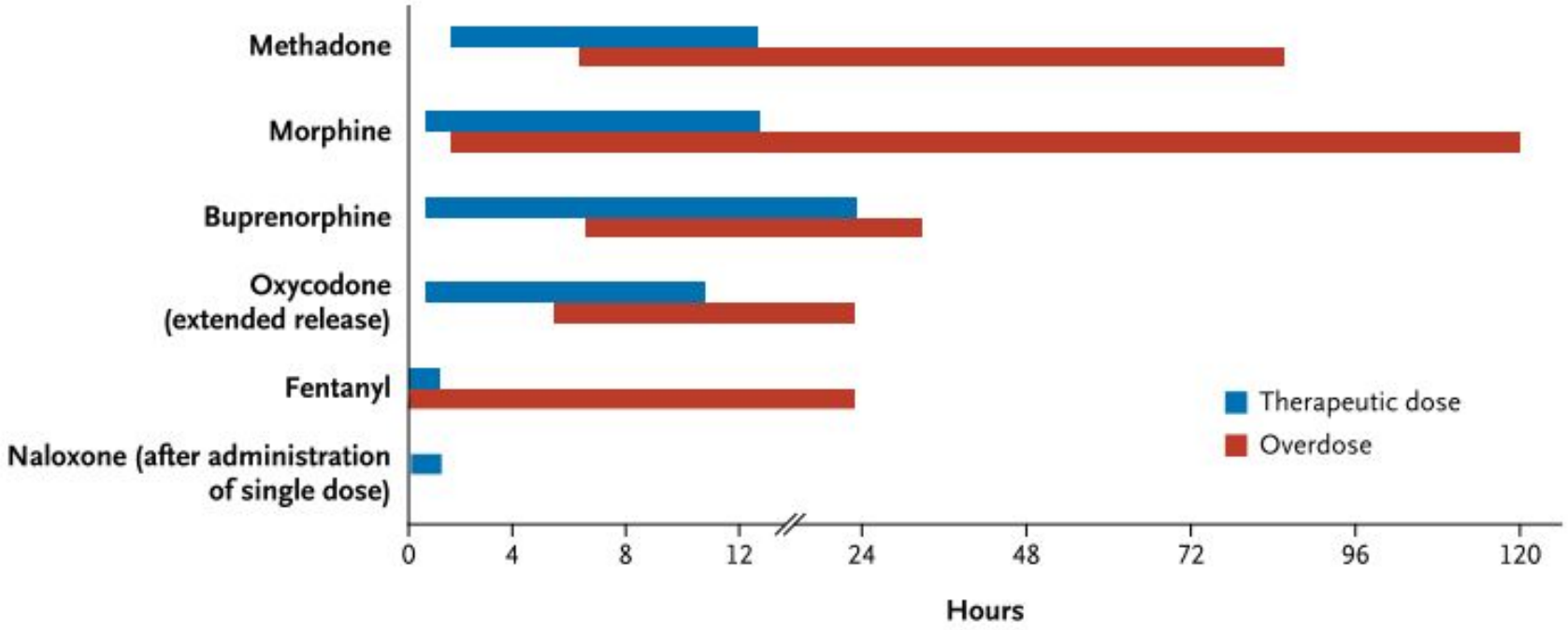
FIGURE Fentanyl concentration in colostrum and serum (ng · ml^{-1}) ± standard error of the mean.

Steer 1992, Cohen 2009

Fentanyl - illicit

Amount = Dangerous

- Increased plasma concentration, free fraction, and duration



Boyer 2012

Fentanyl

Toxicity (infant susceptibilities)

- Immature respiratory control centers
- Higher amount at target tissue
  - Immature blood brain barrier
  - Higher free drug fraction
  - Decreased PGP
- Increased concentration of mu receptors
- Anatomic differences in airway
- Decreased clearance

van den Anker 2018, Anderson 2021

Fentanyl

Duration

- Boyer – a day in moms who use recreationally
- Steer – 6 hours in milk for moms in surgery
  - Still present at low levels at 24 hours in other references

Boyer 2012, Steer 1992

Fentanyl

Duration

- Boyer – a day in moms who use recreationally
- Steer – 6 hours in milk for moms in surgery
  - Still present at low levels at 24 hours in other references

Drug and Alcohol Dependence 214 (2020) 108147

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Short communication

Protracted renal clearance of fentanyl in persons with opioid use disorder

Andrew S. Huhn[a,b,*], J. Gregory Hobelmann[a,b], George A. Oyler[c], Eric C. Strain[a]

Boyer 2012, Steer 1992

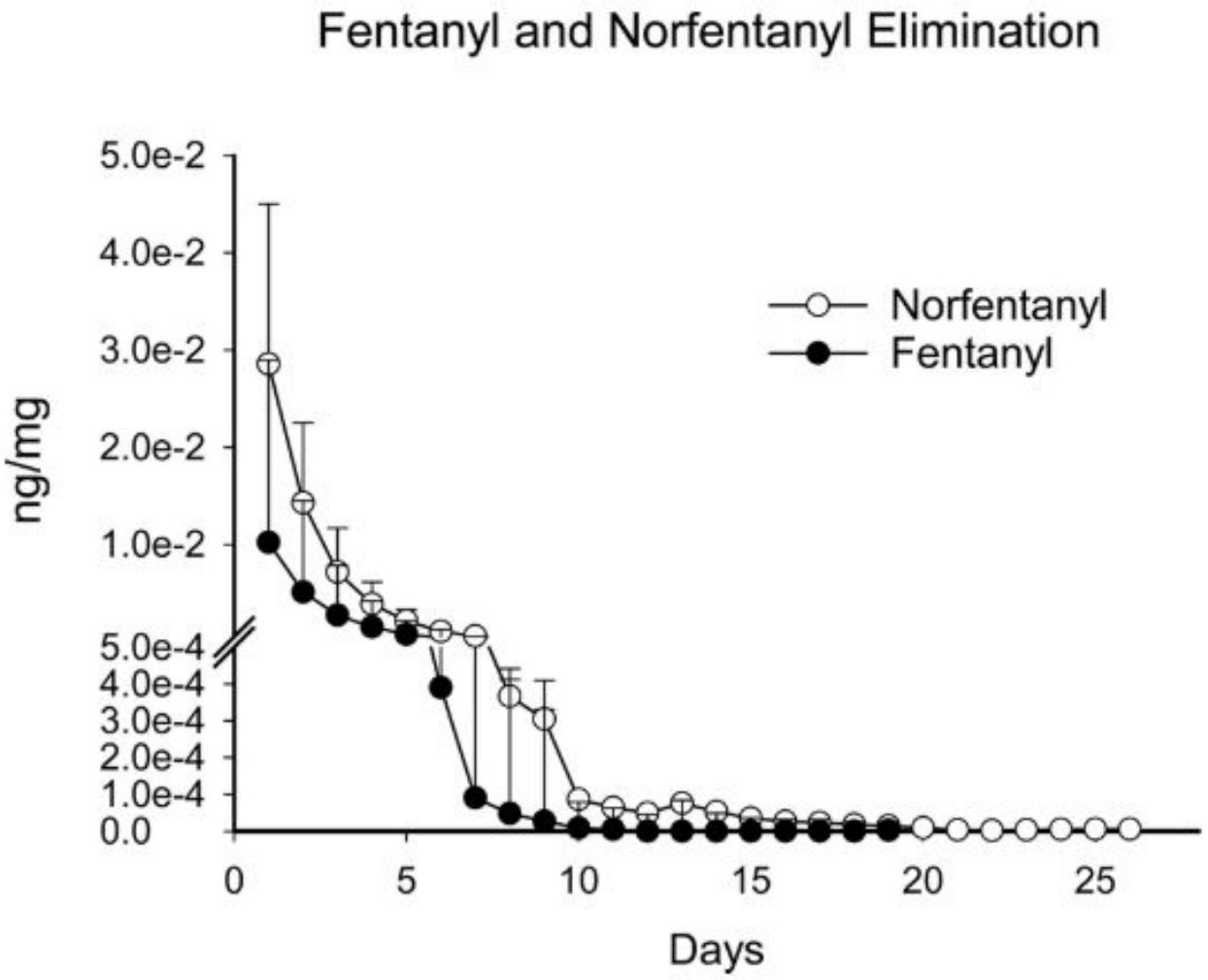
Fentanyl

Duration

- Boyer – a day in mom
- Steer + others – 6 – 24 hours after that

- 48hr - 5 days with supervision
- or negative UDS

Drug and Alcohol Dependence 214 (2020) 108147



Huhn 2020

Medications for opioid use disorder

	Methadone	Buprenorphine
M:P	0.4 (SD 0.21)	0.7-2
Concentration	0.05 - 0.22 mg/L	1.4-4.8 mcg/L
AID	0.033 mg/kg/day (range 0.006-0.170	0.72 mcg/kg/day (max)
RID	2.2% (range 0.52-8.8%)	< 1%
Therapeutic dose	0.05 - 0.1 mg/kg q12-24 hours	4-5.3 µg/kg/dose Max=60 µg/kg/day

Bogen 2011 Beauchamp 2019
Jansson 2004

Jansson 2016
Kocherlakota 2014

Clinical Scenario

- Mother with recent methamphetamine use (reported 3 days), UDS on admission positive for fentanyl and methamphetamine

Component	Value	Flag	Range	Units	Status
Amphetamine Ur	POS		<=500	ng/mL	Corrected

Comment:

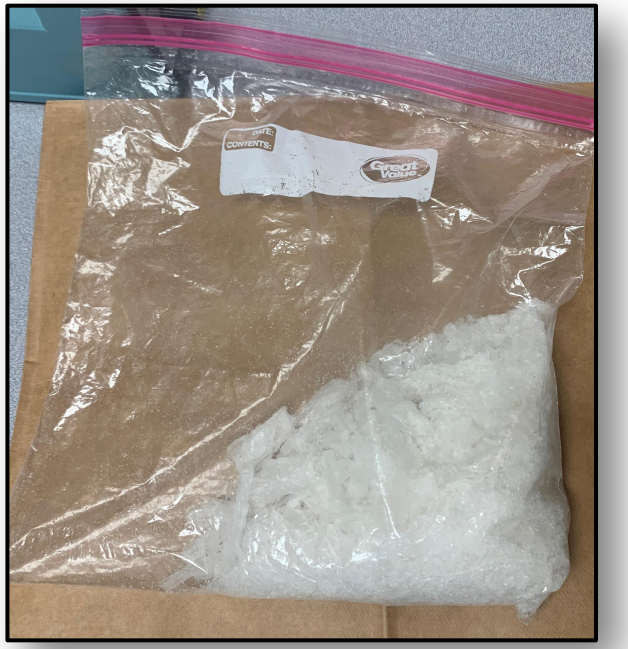
Urine Amphetamine confirmed positive by LC/MS/MS.
The Confirmation Threshold Concentration for Urine Amphetamines
is 50 ng/mL.

Urine Amphetamine = 227 ng/mL
Urine Methamphetamine = 1184 ng/mL
Urine MDA and MDMA = None Detected.
Corrected from PENDING ng/mL [NA] on

Methamphetamine

Amount

- M:P ratio 2-4
- Bartu: 17.5 and 44 mcg/kg/day (IV)
- Chomchai: 21.3 and 51.7 mcg/kg/day (smoked)
- Ilett: 21 mcg/kg/day (Rx dextroamphetamine)
  - RID 5.7% but infants with plasma concentration 6 then 14% of moms'
- Steiner: 14 mcg/kg/day (Rx amphetamine)



Bartu 2019, Chomchai 2016,
Ilett 2007, Steiner 1984

Baby

Acetaminophen Ur	<=10 mcg/mL	NEG	
Amphetamine Ur	<=500 ng/mL	POS !	Urine Methamphetamine present by Mass Spectrometry.
Barbiturate Ur	<=200 ng/mL	NEG	
Benzodiazipine	<=100 ng/mL	NEG	
Buprenorphine Ur	<=5 ng/mL	NEG	
Cocaine Metab Ur	<=300 ng/mL	NEG	
Fentanyl, Urine	<=4 ng/mL	NEG	
LSD Ur	<=500 pg/mL	NEG	
Methadone Ur	<=300 ng/mL	NEG	
Opiate Ur	<=300 ng/mL	NEG	
Oxycodone Ur	<=100 ng/mL	NEG	
PCP Urine	<=25 ng/mL	NEG	
Propox Ur	<=300 ng/mL	NEG	
Salicylate Ur	<=10 mg/dL	NEG	
Creat Urine	>=20 mg/dL	65	
Mass Spectrometry Urine		Lidocaine, Lidocaine metabolite, and Methamphetamine present.	

Normal vital signs

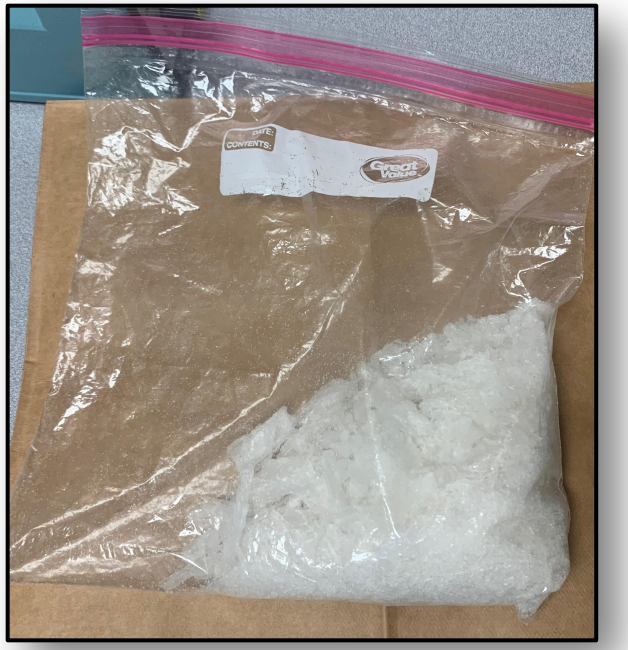
GENERAL: Alert, fusing and frantically waving arms in crib. Soothes quickly then escalates again. Near feeding time.

NEUROLOGIC: Some tremors in the arms when disturbed. Excessive sucking present with loud smacks on pacifier. Frantic and disorganized when trying to root. Passive ROM of extremities feels normal for age, but head lag is absent even when infant calm, indicating relatively high tone.

Methamphetamine

Toxicity

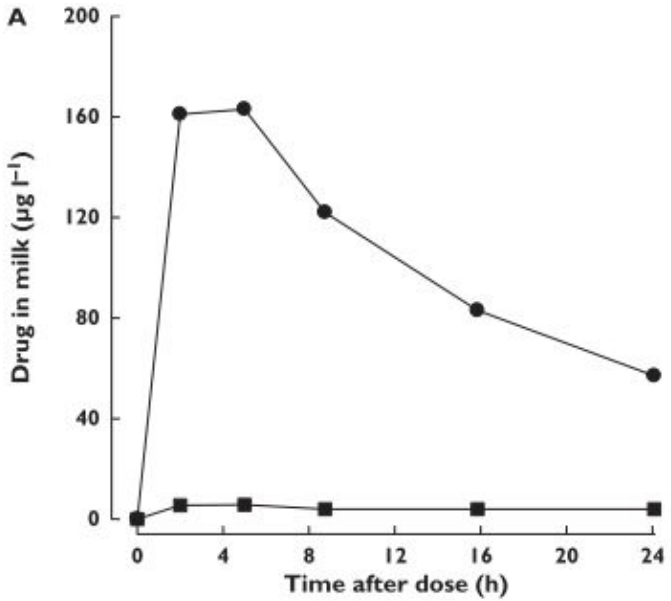
- Acute
  - Ayd 1973: no increased stimulation or insomnia
  - People vs Hendersen 1994
    - Woman convicted of killing infant via meth in breastmilk
- Long term:
  - 7 children in cases “normal”
    - 2 verified by formal assessment



LactMED 2021 (Ayd), Ariagno 1995, Bartu 2019, Ilett 2007, Steiner 1984

Methamphetamine

- Duration - Bartu 2009
  - present 48 hours,
  - T1/2 7.4h and 13.5h



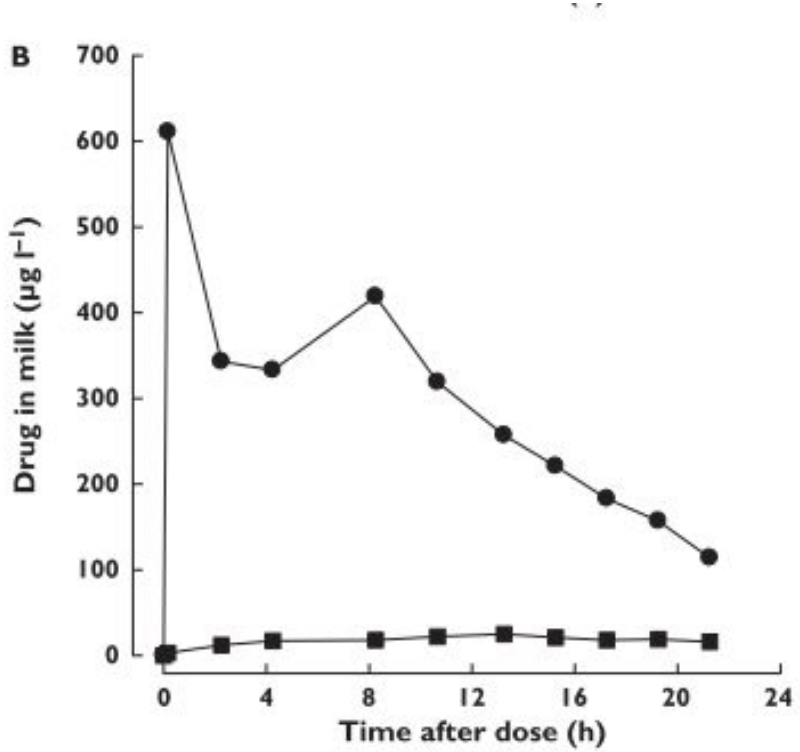


Figure 1

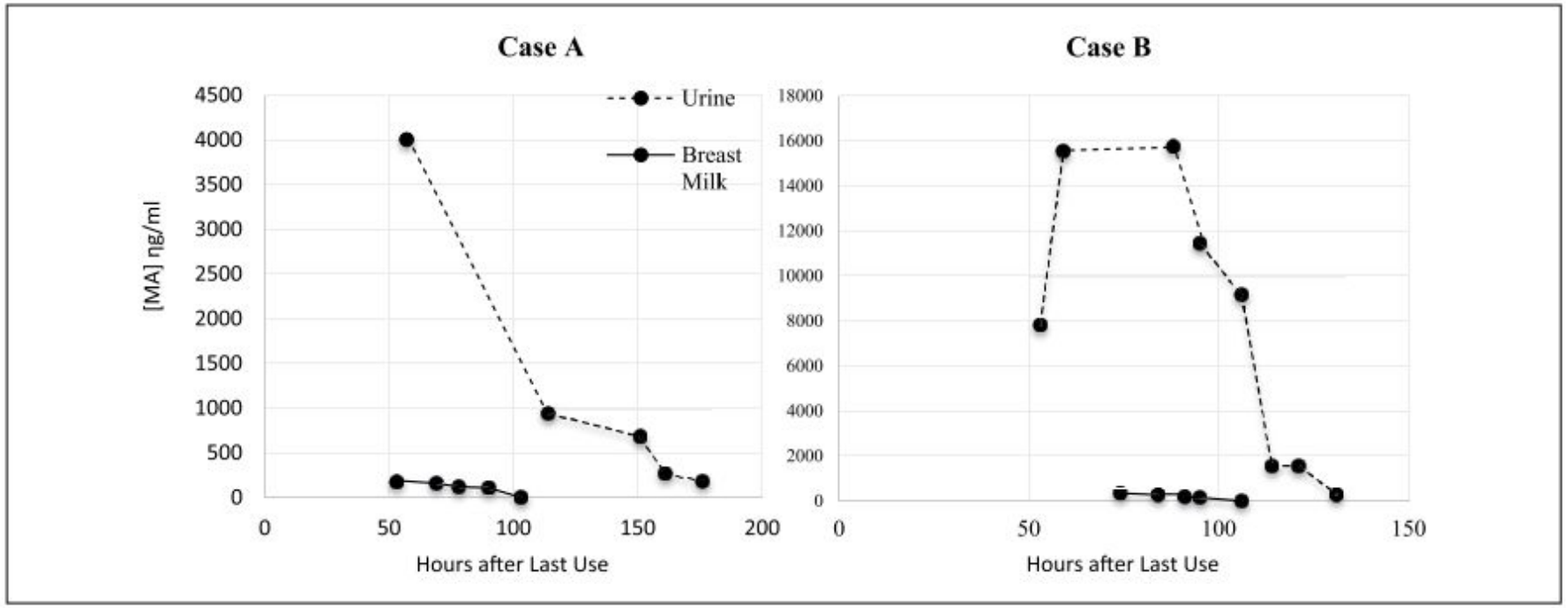
Drug concentration in milk *vs.* time for case 1 (a) and case 2 (b) following self-administration of one 'point' of methylamphetamine at zero time. methylamphetamine (●); amphetamine (■)

Methamphetamine

Duration – Chomchai 2016

- present 100+ hours

Figure 2. Methamphetamine Concentations ([MA]) in Urine and Breast Milk versus Hours after Last Methamphetamine Use for Cases A and B.



Mom – DOD and 2 days later

Component	Value	Flag	Range	Units	Status
Amphetamine Ur	PENDING		<=500	ng/mL	Final
Barbiturate Ur	NEG		<=200	ng/mL	Final
Benzodiazipine	NEG		<=100	ng/mL	Final
Cocaine Metab Ur	NEG		<=300	ng/mL	Final
Methadone Ur	NEG		<=300	ng/mL	Final
Opiate Ur	NEG		<=300	ng/mL	Final
Oxycodone Ur	NEG		<=100	ng/mL	Final
PCP Urine	NEG		<=25	ng/mL	Final
THC Ur	PENDING		<=50	ng/mL	Final

Component	Value	Flag	Range	Units	Status
Amphetamine Ur	POS		<=500	ng/mL	Corrected

Comment:

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Acetaminophen Ur	<=10 mcg/mL	NEG
Amphetamine Ur	<=500 ng/mL	NEG
Barbiturate Ur	<=200 ng/mL	NEG
Benzodiazipine	<=100 ng/mL	NEG
Buprenorphine Ur	<=5 ng/mL	NEG
Cocaine Metab Ur	<=300 ng/mL	NEG
Fentanyl, Urine	<=4 ng/mL	NEG
LSD Ur	<=500 pg/mL	NEG
Methadone Ur	<=300 ng/mL	NEG
Opiate Ur	<=300 ng/mL	NEG
Oxycodone Ur	<=100 ng/mL	NEG
PCP Urine	<=25 ng/mL	NEG
Propox Ur	<=300 ng/mL	NEG
Salicylate Ur	<=10 mg/dL	NEG
Creat Urine	>=20 mg/dL	30
Mass Spectrometry Urine		Acetaminophen, Amphetamine, Ibuprofen, and Methamphetamine present.

Clinical Scenario

- Mother with alcohol use disorder admitted in alcohol withdrawal then labor.
- Feels “already harmed baby enough” so does not want to breastfeed given medications she’s on for withdrawal and starting back on naltrexone.

Summary

- Breastfeeding benefits are significant and substantiated
- Drugs transmit into breastmilk differently
- Literature around drug excretion and potential infant toxicity for several substances is challenging and often limited to case reports.
  - Data on long-term outcomes may never be possible
- Use the known benefits and the data we have about risk to counsel women about initiation of breastfeeding and making a plan in case of re-use

	Alcohol	Nicotine	THC	Kratom
Excreted into BM?	Yes	Yes	Yes	
How long is it in BM?	---	---	~85 days	
Intoxication in baby from exposure?			No	
Long term effects in baby?			Motor at 1 year	
Oral bioavailability			4-12%	

	Buprenorphine	Methadone	Fentanyl	Cocaine	Amphetamine
Excreted into BM?	Yes	Yes	Yes	Yes	Yes
How long is it in BM?	---	---	Unknown	36 hours	100 hours
Intoxication in baby from exposure?	No	No	Unknown	Yes	No
Long term effects in baby?	UTA	UTA	Unknown	Unknown	Unknown
Oral bioavailability	15%	36-100%	50-64% TM/buccal	20-60%	75-100%

Questions?

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Resources:

- Sachs HC. The transfer of drugs and therapeutics into human breast milk: An update on selected topics. *Pediatrics*. 2013;132(3)
- LactMED® NIH Drugs and Lactation Database
  - LactRx app

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PubChem

Drug	Molecular weight	pKa	LogP	Protein binding*
Fentanyl	336.5	8.43	4.5	80-85%
Cocaine	303.35	8.7	2.3	90%
Methamphetamine		9.99	2.07	Amphetamine 20%
Diacetylmorphine	369.4	7.96	1.58	None (morphine 20-30%)
THC	314.5	10.6	5.65	Dronabinol 97% (99 per ryan et al)
Alprazolam	308.8		2.12	80%
Etizolam	342.8		2.6?	
GHB	104.1	4.72	-0.6	None
Ethanol	46.07	15.9	-0.31	
LSD	323.4	7.8	2.95	80%
PCP	243.4	8.29	4.69	
Ketamine	237.72	7.5	~3	53%
Kratom (mytragynine)	398.5	Weak base?	3.4?	

https://pubchem.ncbi.nlm.nih.gov/

Edwards *Pharm Res* 1988

Neavyn in *Goldfranks* 2019

*Concentration dependent

- Don’t forget the why when discussing abstinence/decreasing use . . .

Approach to Counseling Mothers is Important (Courtesy of Dr. Christine Murphy)

Marijuana Counseling Domains: Definitions and Examples

Domain	Definition and Example
No counseling	No health care provider response to patient's marijuana use or disclosure; health care provider may assess last use if patient quit since confirming pregnancy but offers no information or counseling regarding marijuana use.
	OB: Any smoking, drinking, or drugs? **PT:** I smoked marijuana a month ago to 2 months ago. **OB:** And how much did you used to smoke? **PT:** Marijuana? **OB:** No, cigarettes. **PT:** Ah a pack would last me for 2 weeks. **OB:** Alright Ms. X. So again it is your first time seeing us, um, so we are going to do a number of tests that we do for everybody on their first pregnancy visit.
Punitive	Counseling focused on the legal ramifications of patient's marijuana use; patient wamed child protective services will be contacted or informing patient that urine drug screening will be performed (at visit; at delivery).
	OB: Um, the issue with marijuana specifically is just that it is illegal. So at the time of delivery, they will do a urine drug test because you have a history of using it. If it is positive, at the time of delivery, they will often have you, like force you to talk to the child protective services because it is a risk factor.
Medical	Counseling focused on medical risks of marijuana use such as comparing the negative outcomes of smoking tobacco (small gestational age, preterm birth, asthma); includes discussions regarding nausea and suggestions of using or prescribing medications for nausea in place of marijuana.
	OB: We do know it can affect size of the babies and things like that. And we want your baby to develop as healthy as possible. And you know how it alters your mind when you have it, how it makes you feel, so think about what it is doing to the baby that is not even formed quite yet. It gets the effects as well. And we don't want to do that to the baby.
Helpful and supportive	Counseling included offering resources such as social work or counseling referrals, providing encouragement and support to quit; health care provider notes intention to follow-up with patient on quit efforts.
	OB: If you find yourself in a position where you feel like you can't stop using…there are lots of avenues that we can help you explore to…keep you clean and sober…So let us know if there is anything we can do to help.
Unclear	Counseling is not specific, health care provider expressed uncertainty of effects of marijuana use during pregnancy, patients advised to quit without providing information on risks or other educational information.
	OB: Ok, so our goal is to keep you off of everything during pregnancy.

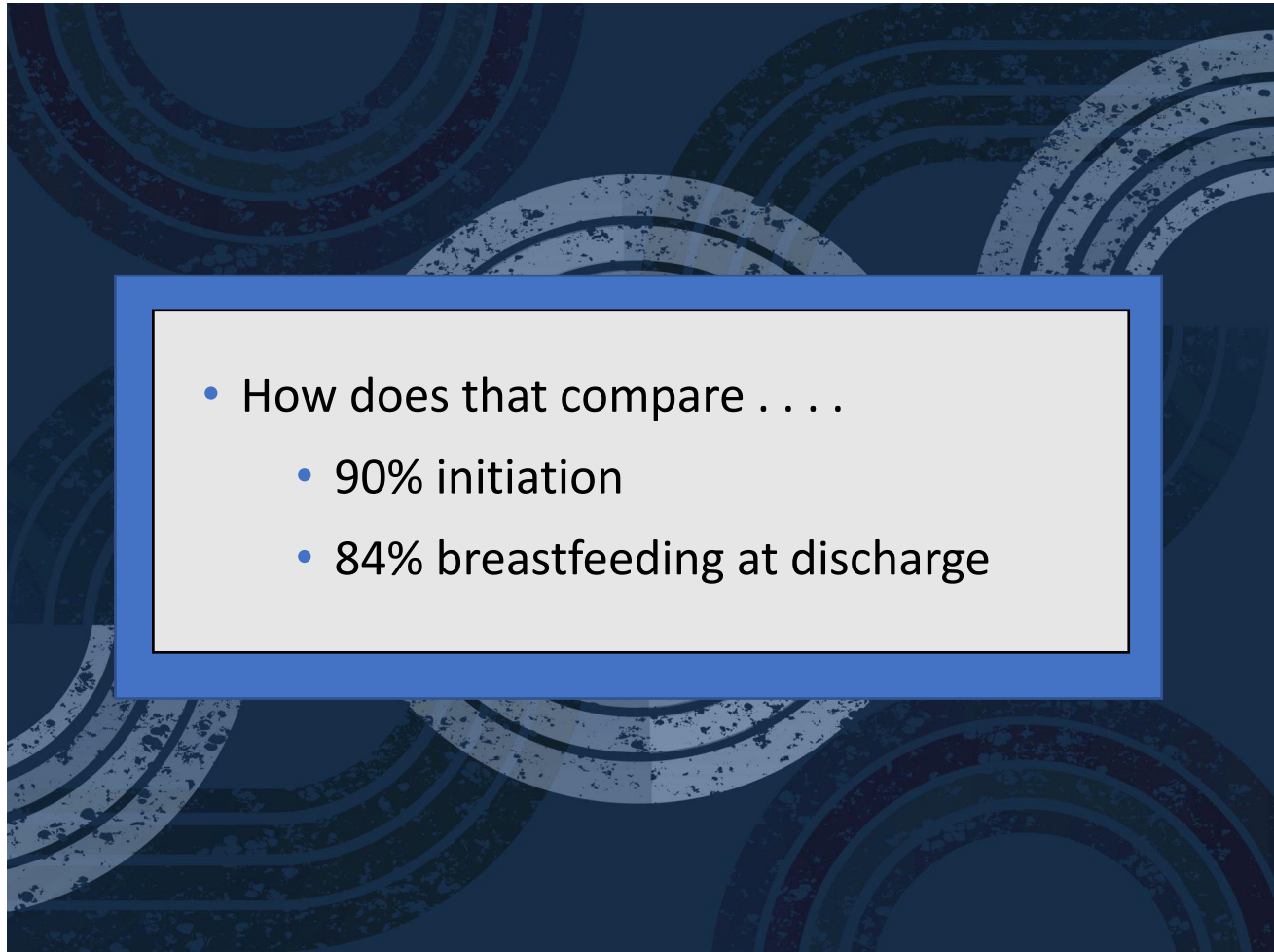
- Are we doing a good enough job?

Encouraging Moms with SUD to Breastfeed

Initiating Breastfeeding

- Methadone
  - 71% initiated breastfeeding in hospital
  - 19% breastfeeding on discharge

- Buprenorphine
  - 82% initiated breastfeeding in hospital
  - 31% breastfeeding on discharge



Encouraging Moms with SUD to Breastfeed

- Are we doing a good enough job?
- Do we exhibit biases towards mothers with SUD?
- What is our messaging to mom about breastfeeding?

	Buprenorphine	Methadone	Fentanyl	Cocaine	Amphetamine	MJ
Excreted into BM?	Yes	Yes	Yes	Yes	Yes	Yes
How long is it in BM?	---	---	Unknown	36 hours	100 hours	~85 days
Intoxication in baby from exposure?	No	No	Unknown	Yes	No	No
Long term effects in baby?	UTA	UTA	Unknown	Unknown	Unknown	Motor at 1 year
Oral bioavailability	15%	36-100%	50-64% TM/buccal	20-60%	75-100%	4-12%

Clinical Scenario (Pic on right)

- Patient

Substance

Amount

- M:P

- RID
- AID

refe

Substance

Toxicity

Ref

Long-term toxicity?

Ref

Substance

Duration

- # days

Ref

Nicotine


Before you scold me, Mom ...
maybe you'd better light up a
Marlboro
Yes, you need never feel over-smoked .... that's the Miracle of Marlboro!
MARLBORO
Gee, Mommy you sure enjoy your
Marlboro
Yes, you need never feel over-smoked .... that's the Miracle of Marlboro!
MARLBORO